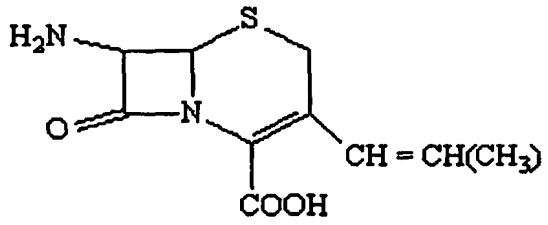
WE CLAIM:

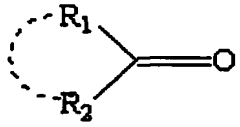
1. A process for the preparation of (Z)-isomer-enriched 7-amino-3-(1-propen-1-yl)-3-cephem-4-carboxylic acid of Formula I,



FORMULA I

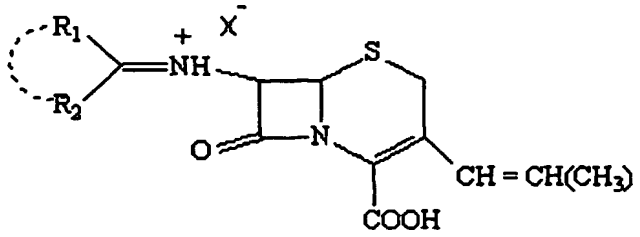
the process comprising:

(a) reacting a mixture of the (Z)- and (E)- isomers of carboxylic acid of Formula I with a compound of Formula II



FORMULA II

wherein R_1 and R_2 are independently hydrogen, alkyl, alicyclic, aryl, aralkyl, or R_1 and R_2 together form a 5- to 7-membered carbocyclic ring, in the presence of an acid, HX, to form a reaction mixture comprising an alkylidene ammonio salt derivative of Formula III,



FORMULA III

wherein R_1 and R_2 are the same as above and X^- is an anion from the acid HX;

(b) obtaining (Z)-isomer-enriched alkylidene ammonio salt derivative of Formula III from the reaction mixture; and

(c) converting the (Z)-isomer-enriched alkylidene ammonio salt derivative of Formula III to 7-amino-3-(1-propen-1-yl)-3-cephem-4-carboxylic acid of Formula I, as the free acid or in salt forms.

2. The process according to claim 1, wherein the compound of Formula II comprises a ketone.

3. The process according to claim 2, wherein the ketone is selected from one or more of acetone, methyl isobutyl ketone, cyclohexanone, cyclopentanone, and benzophenone.

4. The process according to claim 1, wherein the compound of Formula II comprises an aldehyde.

5. The process according to claim 4, wherein the aldehyde is selected from one or more of benzaldehyde, acetaldehyde and formaldehyde.

6. The process according to claim 1, wherein the acid comprises an inorganic acid.

7. The process according to claim 6, wherein the inorganic acid comprises one or more of hydrogen chloride, hydrogen bromide, hydrogen iodide, sulfuric acid and perchloric acid.

8. The process according to claim 1, wherein the acid comprises an organic acid.

9. The process according to claim 1, wherein the organic acid is selected from one or more of formic acid and acetic acid.

10. The process according to claim 1, wherein the reaction is performed in an inert non-aqueous organic solvent or solvent mixture in which the (Z)- and (E)- isomers of the derivative of Formula III have different solubilities.

11. The process according to claim 10, wherein the organic solvent or mixture is such that the (Z)-isomer of the salt derivative of Formula III is relatively insoluble and the (E)-isomer is soluble.

12. The process according to claim 10, wherein the organic solvent or mixture comprises one or more of carboxylic acids, amides, sulfoxides, sulfones, halogenated hydrocarbons, ketones, esters, ethers, and nitriles.

13. The process according to claim 11, wherein the organic solvent or mixture comprises one or more of acetic acid, dimethylformamide, dimethylsulfoxide, sulfolane, dichloromethane, acetone, ethyl acetate, tetrahydrofuran, and acetonitrile.

14. The process according to claim 1, wherein the reaction mixture of step (a) is diluted with a counter solvent or a mixture of counter solvents to obtain the (Z)-isomer enriched derivative of Formula III.

15. The process according to claim 14, wherein the organic counter solvent comprises one or more of ketones, ethers, esters, and nitriles.

16. The process according to claim 15, wherein the organic counter solvent comprises one or more of acetone, tertiary butyl methyl ether, diethylether, tetrahydrofuran, ethyl acetate, isopropyl acetate, and acetonitrile.

17. The process according to claim 1, wherein the reaction of step (a) is performed at a temperature of between about 20°C to about 55°C.

18. The process according to claim 17, wherein the reaction is performed at a temperature of between about 30°C to about 45°C.

19. The process according to claim 1, wherein obtaining the (Z)-isomer-enriched alkylidene ammonio salt derivative of Formula III comprises crystallizing the derivative of Formula III at a temperature of between about 0°C to about 30°C.

20. The process according to claim 19, wherein the (Z)-isomer-enriched alkylidene ammonio salt derivative of Formula III is crystallized at a temperature of between about 0°C to about 15°C.

21. The process according to claim 1, wherein conversion of the carboxylic acid of Formula I provides the compound of Formula I comprising Z/E isomers in a ratio of about 91:9 to about 99:1.

22. The process according to claim 1, further comprising converting the (Z)-isomer-enriched carboxylic acid of Formula I to a 3-propenyl cephalosporin antibiotic.

23. The process according to claim 1, further comprising converting the (Z)-isomer-enriched carboxylic acid of Formula I to cefprozil.

24. The process according to claim 23, wherein cefprozil comprises Z/E isomers in a ratio of from about 91:9 to about 99:1.

25. The process according to claim 1, further comprising obtaining cefprozil by:

silylating the (Z)-isomer enriched 7-amino-3-(1-propen-1-yl)-3-cephem-4-carboxylic acid of Formula I; and

reacting the silylated product with a mixed carboxylic acid anhydride produced by reacting a Dane salt with ethyl chloroformate.

26. A drug product comprising a 3-propenyl cephalosporin antibiotic formed by the process of claim 22.

27. A drug product comprising cefprozil formed by the process of claim 23.

28. A drug product comprising cefprozil formed by the process of claim 24.

29. A drug product comprising cefprozil formed by the process of claim 25.

30. A method of treating a condition for which an antibiotic is indicated, the method comprising providing a drug product comprising a 3-propenyl cephalosporin antibiotic formed by the process of claim 22.

31. The method of claim 30, wherein the 3-propenyl cephalosporin antibiotic comprises cefprozil.